Testimony for the Record
Submitted to the
House Committee on Appropriations
Subcommittee on Interior, Environment and Related Agencies

Peter Larsen, PhD

Assistant Professor of Molecular Biology, College of Veterinary Sciences
at the University of Minnesota

Chairwoman McCollum and Ranking Member Joyce, and Members of the Subcommittee on Interior, Environment and Related Agencies, thank you for inviting me to participate in today's hearing. It is an honor to appear before you.

I am an Assistant Professor of Molecular Biology at the University of Minnesota College of Veterinary Medicine. My academic career has focused on wildlife biology and the genetics of wild mammals. I use emerging genomic technologies to facilitate a wide variety of scientific research projects, ranging from mammalian genome assembly to the discovery of new diseases circulating in wildlife. A central component of my research program at the University of Minnesota is the application of cutting-edge genomic tools to challenging biological questions. Chronic Wasting Disease (CWD) represents one of the most challenging wildlife diseases we have ever faced. I am leading a research team's effort at the UMN to develop new CWD diagnostics, while also educating students and the public about the biology of CWD.

Background

CWD is a contagious and 100% fatal neurodegenerative disease affecting cervids such as deer, moose, elk, caribou, and reindeer. Within the United States, CWD likely originated in Colorado during the 1960's and the disease has since spread to 26 US states in both wild and farmed cervids (USGS National Wildlife Health Center). It is critical to understand that CWD belongs to a family of well-known prion diseases that include scrapie in sheep, bovine spongiform encephalopathy in cattle, and Creutzfeldt-Jakob disease in humans. Decades of robust scientific research has shown that the pathogenic agent of CWD is a misfolded prion protein. This misfolded CWD-causing prion is spread by both direct (animal to animal) and indirect (environment to animal) routes and CWD positive cervids can serve as a source of infectious prions for up to 88% of their infected life. Infected animals can begin shedding these misfolded prions into the environment very soon after infection, though saliva, blood, feces, and urine and their carcasses can also serve as a source for new CWD infections. One of the most challenging aspects with respect to the management of CWD is that the infectious prions are resistant to degradation and it is believed they can remain infectious for years within the environment. Moreover, the progression of the disease is slow and infected animals can go months before displaying obvious symptoms thus complicating control strategies.

CWD represents an immediate threat to our Nation's cervid populations. This is not a trivial observation, for many reasons. CWD is already damaging regional economies across the United States, and a looming risk is the potential for negatively impacting the sale of agricultural commodities produced from CWD endemic areas. However, when considering the damage that CWD represents to our country, there is another, equally important issue at stake that deserves attention. This is the expansive heritage that unites humans with cervids in North America and beyond. Humans have been interacting with deer in North America for thousands upon thousands of years. For this reason, we are inherently connected with cervids, it is part of the lifeblood for all those that call North America home. CWD represents a devastating threat to that heritage. Our Nation's cervids are under attack and we must mobilize now to save them.

Formation of Cross-disciplinary Research Teams

It is clear the only way that we ultimately defeat CWD is by tapping into our nation's broader technological and intellectual resources. A newly formed CWD Research Consortium (NCDC234) composed of government, academic, and industry scientists, representing natural resource management, animal, and human health sectors, provided further support that a collective approach to this complex problem is the only solution. We need to provide those tasked with managing the spread of CWD with new resources to protect deer heritage. It is essential that the greater scientific community act with urgency to work collectively and develop new tools and approaches that can aid in this fight. These include advanced CWD diagnostic procedures, environmental remediation strategies, evidence-based management, and vaccination and therapeutic approaches that can be deployed in the fight against CWD.

With respect to academic institutions across the United States, we need to foster the formation of collaborative research teams who would perform cutting-edge research aimed at better understanding the biology and epidemiology of prion diseases and related protein-misfolding disorders. These teams would serve as research incubators and think-tanks with a collective mission of generating transformative insights across the entire spectrum of neurodegenerative disease. Specific CWD-related research thrusts should include the development of advanced prion decontamination strategies, rapid CWD diagnostic approaches, ecological remediation strategies, vaccine development, geographic predictive modeling, human dimensions in management and control, and the assessment of the zoonotic potential of CWD.

These teams should collaborate directly with Federal, Tribal and State-level agencies to understand the situation on the ground and the lessons learned in the decades long fight against CWD, and any research discoveries must be shared directly to both federal and state-level stakeholders tasked with managing CWD across the country. Although initially formed under the umbrella of an emerging prion disease of wildlife, such research incubators would have a sustained and long-term impact across a wide variety of research areas. A clear example is the potential for transformative insights into a number of neurological diseases in humans that center on the misfolding of proteins, including Alzheimer's disease, Parkinson's disease, and ALS.

Our University of Minnesota scientific team, has proposed the formation of a cutting-edge think tank that would serve as a hub for both combatting CWD and performing fundamental research on prions and protein-folding diseases. Staff and faculty of the Minnesota Center for Prion Research and Outreach (MNPRO) would be dedicated to devising innovative technologies and strategies to combat the spread of CWD across the United States. We will leverage our collective strengths in wildlife biology, epidemiology, genomics, and biotechnology and will collaborate with other academic institutions and both State and Federal entities to solve critical issues surrounding the management of CWD. One of the most important areas of research that our MNPRO team will focus on is the development of advanced CWD diagnostic tools.

New Diagnostic Tools

Despite the relentless spread of CWD and the potential for a catastrophic impact on cervid heritage and cervid-related industries, diagnostic tools for the detection of CWD remain limited. Currently available CWD diagnostic tests are hampering our collective ability to rapidly identify and manage the spread of the disease. These tests are cumbersome, expensive, they require significant technical expertise, and they can take days to complete. Moreover, confirmatory tests largely require specific tissues from euthanized deer to identify CWD prions. For these reasons, hunters who want to test their deer for CWD must endure a wait time before knowing whether or not their harvest is safe to eat. Those who manage farmed deer populations do not have access to a robust test that can be used with live animals. Those who monitor CWD in the wild do not have a rapid and sensitive test capable of providing real-time information from deer carcasses or from the environment. And it is not currently feasible to screen for CWD prions in taxidermy facilities or within facilities that process venison for human consumption. Indeed, the September 2019 meeting of the CWD Research Consortium identified the need for rapid diagnostic technology as a key priority.

The available “gold-standard” CWD diagnostic tests are based on aging technology and they require upgrading. To this end, it is important to note that the field of molecular diagnostics has witnessed spectacular technological advancements over the past few years. Many of these advancements are rooted in emerging genomic technologies that center on microfluidics and nanotechnology. I cannot emphasize enough how the fields of molecular biology and genomics have been impacted by emerging technologies. A clear example is found with the original assembly of the human genome. Scientists began working on the human genome project in 1990 and the effort was completed 13 years later at a total cost of approximately $3 billion dollars. Now, in 2019, I use newly developed DNA sequencing technology in my laboratory and I can sequence a human genome over the course of two or three days at the cost of approximately $1,000. Moreover, this technology is the size of a candy bar, it fits in the palm of my hand and it is portable. The technology is the Oxford Nanopore MinION sequencer, and my lab utilizes this machine for a number of wildlife-based research projects, including molecular diagnostics using DNA and RNA. We need to adapt these technologies for protein-focused diagnostics and this is what is needed in the CWD diagnostic realm.

This research area, that of molecular diagnostics, is primed and ready for the rapid advancement of CWD diagnostics. It is essential that scientists leverage recent advancements in microfluidics and nanotechnology for the rapid, sensitive, and accurate detection of the misfolded prion proteins that are the causative agent of CWD. There are clear research lines that can be pursued in this area and over the past year our research team has secured over $2M of state-level funds to support the development of new CWD diagnostic tools. This investment by the Minnesota state legislature is already having a domino effect across the CWD research arena. Michigan has just recently announced a $900K investment to Michigan State University for the development of next-generation CWD diagnostic tools.

With respect to our ongoing efforts in the state of Minnesota, we are also collaborating with Native American tribal nations led by the Grand Portage Band of Lake Superior Chippewa and five additional tribes. We have recently secured funding to establish a Tribal CWD surveillance network, which will incorporate Tribal priorities in CWD management and augment ongoing surveillance efforts by the Minnesota Department of Natural Resources.

Collectively, these investments are uniting a broad community of stakeholders and scientists to work on the common problem of CWD surveillance. It is this mechanism, this uniting of experts from diverse backgrounds, that will result in the development of unique approaches to CWD detection and that would be an enormous step forward in the battle against CWD.

Development of Genomic Resources

There is another critical area of research that, if expanded upon, would aid in the fight against CWD. This is the expansion of genomic resources for cervids through the availability of high-quality genome assemblies. These genomes must consist of robust datasets for caribou, elk, moose, mule-deer, white-tailed deer, reindeer and closely related cervid species. How would the availability of these genomes aid in our fight against CWD? Providing scientists access to high-quality genomes opens a vast array of potential research lines, including the development of CWD vaccines and therapeutic interventions. The recent advancement in genomic technologies, described above, has made it possible for small research teams to assemble and describe the genomes of cervids.

As of today, genome assemblies exist for just a handful of cervids (e.g., mule deer, white-tailed deer, red deer), but these should be improved and expanded upon using newly released genomic tools. We can use these genomes to better understand the genetic variation across cervids and to make insights into the cervid immune system, this is essential for downstream vaccine development. Because CWD impacts many cervid species, the development of effective CWD vaccines and therapeutics must incorporate the genetic variation observed across those species. Thus, multiple genomes across the entire cervid family would allow for novel comparative analyses, information that is critical for those tasked with developing novel interventions.

Beyond genome assemblies, there are additional genomic resources that would benefit the fight against CWD. These resources would consist of curated frozen tissue collections that would house samples of all cervids found in North America and would include both CWD positive and negative material. The establishment of a national CWD tissue database and repository for CWD transmission and pathogenesis research was identified as one of the top research priorities during the September 2019 CWD Research Consortium meeting.

We need to secure and curate frozen tissue samples from across the geographic distribution of each cervid species in North America. Such a bio-repository would provide biologists with the material required to examine prion-strain variation within the

natural cervid populations throughout the country. This understanding would provide critical information across a number of research areas, including the identification of genotypes resistant to CWD and any prion strains that might be of concern to human health. Our nation's natural history collections, such as those at the Smithsonian, are a critical component of this research area. Mammalogists have been collecting tissues from cervids across the United States for many years and these tissues can now be used to help us in our ongoing battle against CWD.

Closing Remarks

We are at a critical moment in the fight against CWD. I believe that the federal and state-level agencies tasked with managing CWD across the USA have done an exceptional job. However, we need to provide them with an expanded repertoire of tools that could help them win the war against this emerging disease. At minimum, these tools should include new diagnostic techniques for the rapid and reliable detection of CWD and the development of genetic resources of cervids to prepare for broad scale therapeutic interventions. In order to accomplish this, we need to leverage the diverse research-strengths present within our academic institutions. We must encourage the formation of cross-disciplinary CWD research teams, organized specifically to conduct transformative research. These teams should be provided with the resources needed to perform cutting-edge research aimed at protecting the heritage that surrounds the cervids of North America, and beyond.

Thank you for the opportunity to share my perspective on this issue. I am happy to provide you with any additional information and I look forward to further discussion on this important topic.